Reviewer #1: Firstly, I would like to congratulate you by the submitted paper. The information provided is useful to a better knowledge and diffusion in Stem Cells Therapies for diabetic wound healing. Maybe I would like you to develop more deeply some aspects in your paper. In the following sections, aspects I consider modifiable or revisable of the submitted manuscript will be highlighted. The presented paper is a mini-review, but I think it could be interesting to present some data about methodology and literature searching: • What is the methodology of this manuscript briefly? • How many research papers have been published in the field? • How many registered ongoing clinical trials are active (i.e clinicaltrials.gov or similar registries). In the INTRODUCTION section: • I suggest to modify the sentence to "the progression of diabetic wounds can be accelerated, often resulting in complications demanding an amputation. In the SC THERAPIES FOR DIABETIC WOUNDS IN CLINICAL WORK: • Because they are mentioned in the conclusions, and is presented in the table, a paragraph could be added to explain the routes and ways of administration: topical, intravascular, intralesional or combinations. • It could be interesting to mention one meta-analysis in the field and its results (Guo J, Et al. Meta-analysis on the treatment of diabetic foot ulcers with autologous stem cells. Stem Cell Res Ther. 2017 Oct 16;8(1):228. doi: 10.1186/s13287-017-0683-2). • The possibility of modifying or pre-treatment of stem cells has been explored and published and could be mentioned (Amini A. DOI: 10.1007/s10103-021-03451-6) and also that SCs have demonstrated their therapeutic potential in the field even if infection is present (Amini A. Mol Biol Rep. 2022 Aug 25. doi: 10.1007/s11033-022-07721-6). In the CONCLUSION AND EXPECTATION section: • I suggest to be less categorical in the first sentence and modify it to "Stem Cell therapy could be an effective…" • It is important to mention also that it must be addressed if all SCs are equivalent or maybe some of them could be better than the others in this indication. • Similarly, it could be interesting to mention about cell dosage. It is logical to think that it must be related to wound size. Newly I would like to congratulate authors for their work. Keep working in that way and publishing your research results.

Answer 1: Firstly, we wrote this manuscript by searching and summarizing the literatures published in recent years in PubMed, analyzing the data as well as summarizing conclusions. There are 229 research papers have been published in PubMed. Secondly, there are more than 50 registered ongoing clinical trials in clinicaltrials.gov and one of them are active. And we sincerely accepted your suggestion and made some amendments to the manuscript. Lastly, thank you for your review and comments.

Reviewer #2: This review paper is about the potential use of stem cells in enhancing the healing of diabetic wounds. The abstract needs to be revised as it seems absolutely inappropriate and is not convincing for the reviewer. It is not covering the manuscript that what going to be discussed or reviewed in the text body. The presented literature is unable to completely reflect the ongoing stem cell research, especially the stem cell role in diabetic wound healing. Authors should further focus on exploring the role of stem cells and the underlying mechanisms related to diabetic wound healing. They have only reported that stem cells accelerate diabetic wound healing via enhancing angiogenesis and reducing inflammatory responses. However, what factors contribute to these processes, are important to highlight. Similarly, numerous studies have also demonstrated that stem cell effectively

cured diabetic skin wounds in different animal models and patients clinically then what is the novelty of this review paper? Overall there is nothing important or focused area of wound healing in review, I don't recommend it for publication.
Answer 2: We have expanded and modified the mechanism part of the article, and described the specific details of other categories in detail. And this review aims at summarize the research progress stem cell therapy on diabetic wounds. Thank you for your review and comments.

Reviewer #3: While interesting in the field, this manuscript suffers from several drawbacks in study conception, technical execution and data presentation and, in my opinion, this manuscript in its current shape is not ready for publication. The main issues are as follows: 1- The manuscript must be carefully proofread for grammar, spelling, and punctuation issues. 2- It is recommended that authors improve the design of Tables and Figures. 3- The discussion part is not well written and needs a major rewrite. There is no balance between the different sections of the manuscript. 4- Despite much data in this field, the mechanism of action of stem cells is not well described.
Answer 3: We added more detailed research data and conclusions to the mechanism as well as the discussion part and diagram of the manuscript. At the same time, we reviewed the manuscript again and corrected some errors in expression. Thank you for your review and comments.

Reviewer #4: In this review, the authors systematically describe the mechanism of stem cell therapy for diabetic foot ulcers, the current preclinical and clinical research progress, and the problems and challenges faced by stem cell therapy for diabetic foot ulcers in the future. Although the author has done a lot of work on the content of the article, I would like to make some important suggestions on some key issues to help the author improve the quality of the current manuscript. Major concerns: 1. About the abstract section. "……risks to patients and to diabetic patients." Do you think the patients here are a different group than the diabetics? The application of "and" indicates the parallel and equivalent relation; Please carefully grasp the definition of patient. 2. About "Possible mechanisms of stem cell therapy" section. This paragraph should focus on the pathogenesis of diabetic foot ulcers and lay the groundwork for the subsequent elaboration of the relevant mechanisms of stem cell effectiveness. However, the authors only described some of the pathogenesis of diabetic patients, not the pathogenesis of diabetic foot ulcers. Similarly, in terms of the three mechanisms, only three aspects were mentioned that stem cells can promote angiogenesis function, modulate inflammation and improve the remodeling phase. The description is too general, and the specific molecular mechanism is not described in detail. The regulatory mechanisms of various molecules such as microRNA in promoting healing of diabetic foot ulcers have not been mentioned. 3. About "Stem cell therapies for diabetic wounds in clinical work" section. The authors pointed out that there are a variety of stem cell types and applications for the clinical treatment of diabetic foot ulcers, and there are some side effects. The article did not elaborate on the relevant content in detail. 4. About "Conclusion and expectation" section. The authors mentioned that the therapeutic concentration, the method of use and the method of stem cell collection may affect the therapeutic effect of stem cells

on diabetic foot ulcers, but the current research status of these issues is not discussed in the main text. 5. The main part of the paper is too simple and the discussion part is too complex. Answer 4: In the mechanism part, we added the relevant research on MiRNA, and modified some statements to supplement the main part. At the same time, we added more detailed research data and conclusions to the mechanism as well as the discussion part. Thank you for your review and comments.